

The Claims

This listing of claims will replace all prior versions and listings of all claims in the application.

1-16. (Canceled)

17. (Currently Amended) A mixed TNFSF oligomer comprising:

_____ a) at least one non-naturally occurring variant monomer of a TNFSF protein comprising at least a variant extracellular domain of a said TNFSF monomer protein and a naturally occurring TNFSF protein, wherein said variant TNFSF protein comprises an amino acid sequence that has at least one amino acid substitution in the Large Domain and at least one amino acid substitution in a domain selected from the group consisting of the DE Loop and the Small Domain;

_____ b) and at least one a naturally occurring TNFSF monomer of said TNFSF protein; wherein said mixed TNFSF oligomer has at least a 50% decrease in receptor activation as compared to a homotrimer of said naturally occurring TNFSF oligomer.

18. (Currently Amended) A non-naturally occurring variant TNFSF protein as compared to a naturally occurring TNFSF protein, comprising at least a variant extracellular domain of a said TNFSF protein, wherein said variant TNFSF protein will interact *in vivo* with said a-naturally occurring TNFSF oligomer to form a mixed TNFSF oligomer, and wherein said mixed TNFSF oligomer is substantially incapable of causing ~~has at least a 50% decrease in~~ receptor activation as compared to a homotrimer of said naturally occurring TNFSF oligomer.

19. (Canceled)

20. (Original) A variant TNFSF protein according to claim 18 comprising at least one receptor contact domain that has reduced affinity for a desired receptor as compared to its corresponding wild-type TNFSF protein and retains the ability to interact with other receptor interaction domains.

21. (Canceled)

22. (Original) A variant TNFSF protein according to claim 18, wherein said variant TNFSF protein physically interacts with a naturally occurring TNFSF protein to form mixed trimers.

23. (Original) A mixed TNFSF oligomer comprising at least one variant TNFSF protein monomer according to claim 18 comprising a substitution at a receptor contact position.

24. (Original) A variant TNFSF monomer protein according to claim 18, wherein said variant TNFSF protein comprises a substitution at a trimer interface position.

25. (Original) A variant TNFSF protein according to claim 18, wherein said variant TNFSF protein physically interacts with its corresponding naturally occurring TNFSF protein.

26. (Original) A variant TNFSF protein according to claim 18, wherein said variant TNFSF protein physically interacts with a non-corresponding naturally occurring TNFSF protein.

27-35. (Canceled)

36. (Previously Presented) A variant TNFSF protein according to claim 17, wherein at least one substitution is non-conservative.

37. (Previously Presented) A variant TNFSF protein according to claim 17, wherein at least one substitution is a surface substitution.

38. (Previously Presented) A variant TNFSF protein according to claims 36, wherein said substitution is located within a domain selected from the group consisting of: Large Domain, Small Domain, DE Loop, Trimer Interface and combinations thereof.

39. (Previously Amended) A variant TNFSF protein according to claim 38, wherein at least one of said Large Domain substitutions is at a position selected from the group consisting of TNFA (SEQ ID NO:1) corresponding positions 28, 29, 30, 31, 32, 33, 34, 63, 64, 65, 66, 67, 68, 69, 112, 113, 114, 115, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146 and 147.

40. (Previously Amended) A variant TNFSF protein according to claim 38, wherein at least one of said Small Domain substitutions is at a position selected from the group consisting of TNFA (SEQ ID NO:1) corresponding positions 72, 73, 74, 75, 76, 77, 78, 79, 95, 96, 97 and 98.

41. (Previously Amended) A variant TNFSF protein according to claim 38, wherein at least one of said DE Loop substitutions is at a position selected from the group consisting of TNFA (SEQ ID NO:1) corresponding positions 84, 85, 86, 87, 88 and 89.

42. (Previously Amended) A variant TNFSF protein according to claim 38, wherein at least one of said Trimer interface substitutions is at a position selected from the group consisting of TNFA (SEQ ID NO:1) corresponding positions 11, 13, 15, 34, 36, 53, 54, 55, 57, 59, 61, 63, 72, 73, 75, 77, 119, 87, 91, 92, 93, 94, 95, 96, 97, 98, 99, 102, 103, 104, 109, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 147, 148, 149, 151, 155, 156 and 157.

43. (Original) A variant TNFSF protein according to claim 42, wherein at least one of said Trimer interface substitutions is at a position selected from the group consisting of: 57, 34, and 91.

44. (Original) A variant TNFSF protein according to claim 18, wherein said variant TNFSF protein antagonizes soluble naturally occurring TNFSF proteins.

45. (Previously Presented) A pharmaceutical composition comprising a variant TNFSF protein according to any of claims 17, 18, 20 and 22-26 and a pharmaceutically acceptable carrier.